REMARKS

Applicants respectfully request reconsideration of the present application in view of the remarks that follow.

Status of the Claims

Claims 1-12 are pending with claims 11 and 12 being withdrawn.

The Office Action

1. The Claims are Patentable over Esposito

The PTO states that claims 1-4 and 6-9 are anticipated by Esposito (U.S. Patent publication No.: 2002/0034539). On pages 2 and 3 of the Office action, the PTO supports its rejection by identifying certain sections within Esposito's specification as allegedly teaching the inventive transdermal delivery system. Applicants respectfully disagree with the PTO's conclusions.

As recited by independent claim 1, the claimed transdermal delivery system comprises a drug selected from a recited list in combination with water-miscible tetraglycol and water for dissolving the drug in hydrogel form. According to claim 1, the transdermal delivery system is in the form of a microemulsion which is a system of water, oil, and an amphiphile. Esposito does not teach the inventive system.

As described in the specification many drugs are insoluble in water, even in their ionized forms and require the use of an alcohol to formulate compositions suitable for transdermal applications. See specification at page 3. The claimed transdermal system obviates this problem by permitting the formulation of such drugs in an aqueous medium utilizing water and water-miscible tetraglycol.

Esposito does not teach a transdermal delivery system that is devoid of alcohol nor would Esposito's composition be understood by the skilled artisan to be a microemulsion for at least the following reasons.

Esposito teaches a multicomponent biphasic drug composition that has six components, including a surfactant, co-surfactant and a partition modifying compound to alter the partition coefficient of a drug between the oil and water phase. *Id* at para. 13.

While the Office action has stated repeatedly that the disclosed compositions are microemulsions, the Office's understanding of this term is incorrect. For example, a person of ordinary skill in the relevant art would readily understand the term "microemulsion" to indicate a system of water, oil and amphiphile which is optically isotropic and a thermodynamically stable liquid. See, for example, Danielson & Lindman, *Colloid Surf.*, 3, 391, (1981). Further support that microemulsions are well known in literature for approximately 70 years, and that Esposito's composition would not be understood to encompass microemulsions stems from a 1943 publication in the journal "Nature" disclosing microemulsions to be a clear solution obtained by titrating a normal coarse oil-in water emulsion with a medium chain alcohol or a non-ionized amphipathic substance. See *Nature*, 152:102, (1943), 1st paragraph (attached).

Esposito discloses a composition that contains additional components. Moreover, the components of Esposito's composition, namely, (i) dispersed or internal phase, (ii) dispersing or external phase, (iii) surfactant, (iv) co-surfactant, (v) drug and (vi) a partition coefficient modifier would not result in a microemulsion. This is so because the formation of microemulsions is a specific and controlled process, not only with respect to the components being used to make the microemulsion, but also with respect to the concentration of each component being used. Not all mixtures of oil, water and amphiphiles result in the formation of a microemulsion. Stated differently, while many oil and amphiphiles can form **emulsions** with water, only some can form microemulsions, and only when used in the appropriate proportions. There is no suggestion in Esposito for forming a microemulsion using tetraglycol.

Esposito discloses tetraglycol as a possible component of its transdermal composition. Esposito discloses a composition in which tetraglycol may be chosen amongst other things as a component of the hydrophilic or aqueous carrier. Nowhere does Esposito teach or suggest tetraglycol as the co-surfactant. In fact, the specification and working examples all point to the use of various alcohols and fatty acids as the co-surfactant in Esposito's composition. See para [0078] and claim 9.

The disclosure of alcoholic co-surfactants in Esposito further distinguishes the claimed transdermal system which does not contain alcohol. All of the exemplified compositions in Esposito, however, contain alcohol. Thus, the claimed invention is not anticipated by Esposito and Applicants respectfully request the PTO to withdraw the rejection.

2. Non-obviousness over Esposito in view of Guang Lin

Claim 5 is rejected under 35 U.S.C. § 103(a) as unpatentable over U.S. 2002/0034539 ("Esposito") in view of U.S. Patent No. 5,612,324 ("Guang Lin"). Applicants respectfully disagree.

As stated above, Esposito does not teach the inventive transdermal system. Guang Lin, cited by the PTO to teach a transdermal system comprising a guar-based polymer, does not cure the defects in Esposito.

Guang Lin teaches a method for treating acne using a skin formulation that contains a pharmaceutically acceptable carrier. Guang Lin discloses the pharmaceutical carriers to be a "hydroalcoholic" system, with working examples disclosing compositions that contain between 35 – 40 % weight of an alcohol. See col. 4, lines 31-32 and examples 1-7. Nowhere does Guang Lin teach a transdermal system that is a microemulsion formed of water, oil and amphiphile (i.e., a non-alcoholic system), as claimed.

Although Guang Lim discloses the use of guar gums in transdermal formulations, these gums are mentioned in a list of optional components for thickening the composition. In contrast, the guar-based polymer hydroxypropyl guar hydroxypropyltrimonium chloride is added to the inventive microemulsions to solidify the drug containing liquid to a hydrogel without destabilizing the microemulsion. As described in the specification and further supported by the working examples, the guar-based polymer assists in dissolving or solubilizing the active material in a hydrogel form and facilitates their penetration through skin. See page 5 of published application No. WO 2004/000358 and working examples. These advantages are absent in Guang Lin's formulation. Furthermore, the incorporation of guar-based gum in Esposito's formulation would not result in the claimed transdermal system.

Additionally, since claim 5 depends ultimately from claim 1, it incorporates all of the claim 1 limitations. Therefore, claim 5 is patentable and non-obvious over the combined teachings of Esposito and Guang Lin because these references fail to render claim 1 obvious.

Applicants respectfully request reconsideration and withdrawal of this rejection in view of the above remarks.

3. Non-obviousness over Esposito in view of Dadey

Claim 10 is rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. 2002/0034539 ("Esposito") in view of U.S. Patent 6,417,237 ("Dadey"). Applicants respectfully disagree.

Again, Esposito does not teach or suggest the claimed transdermal system and the addition of a non-ionic surfactant such as a sorbitan monooleate, as taught by Dadey, does not remedy the defects in Esposito. Furthermore, claim 10 ultimately depends from claim 1 and incorporates all its limitations. Claim 10, therefore, is not obvious because the combined teachings of Esposito and Dadey fail to teach the inventive transdermal system.

CONCLUSION

Having advanced credible grounds for overcoming the issues raised in this Office Action, Applicants submit that the present application is now in condition for allowance. Favorable reconsideration is respectfully requested. The Examiner is invited to contact the undersigned attorney should any issues that warrant further discussion remain.

Respectfully submitted,

Date October 8, 2010 By _____

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The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, then the Commissioner is authorized to charge the unpaid amount to the above deposit account. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to the deposit account.